No. 11-725

IN THE
Supreme Court of the United States

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,
Petitioners,

v.

MYRIAD GENETICS, INC., ET AL.,
Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

BRIEF OF KAISER PERMANENTE AS *AMICUS CURIAE* IN SUPPORT OF PETITIONERS

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INTEREST OF *AMICUS CURIAE*[1]

Amicus curiae Kaiser Permanente[2] is the largest private integrated health care delivery system in the United States, providing high-quality, affordable health care services to approximately 8.9 million members in nine states and the District of Columbia.

Kaiser Permanente consists of three different operating entities. Kaiser Foundation Health Plan, Inc.,[3] the nation's largest not-for-profit health plan, and its subsidiary plans provide and administer health care coverage for their members. The not-for-profit Kaiser Foundation Hospitals, which operates 36 hospitals and over 450 other clinical facilities, provides members and other patients with hospital services, either directly or through contractual arrangements. And the eight Permanente Medical Groups, which are physician-owned, consist of more

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[1] Pursuant to Supreme Court Rule 37.6, counsel for *amicus* represents that no counsel for a party authored this brief in whole or in part and that none of the parties or their counsel, nor any other person or entity other than *amicus* or its counsel, made a monetary contribution intended to fund the preparation or submission of this brief. Pursuant to Rule 37.2(a), counsel for *amicus* represents that all parties were provided notice of *amicus's* intention to file this brief at least 10 days before its due date. Pursuant to Rule 37.3(a), counsel for *amicus* represents that all parties have consented to the filing of this brief and that letters reflecting their consent are on file with the Clerk.

[2] "Kaiser Permanente" is not a legal entity but a registered trademark or trade name used by the separate legal entities described above. Unless otherwise indicated, the term "Kaiser Permanente" is used throughout this brief to refer collectively to those entities.

[3] The Kaiser Foundation health plans are providers of health care services as well as health plans, owning and operating facilities where outpatient services are provided and employing many non-physician providers.

than 15,000 primary care physicians, specialists, and geneticists who exclusively provide or arrange for all types of medical care for Kaiser Foundation Health Plan members. In addition to providing medical care, Kaiser Permanente conducts and supports a broad agenda of clinical and health services research through its various research entities. Research has long been a hallmark of Kaiser Permanente and is one of the ways Kaiser Permanente demonstrates its benefits to the communities it serves. Kaiser Permanente conducts research throughout its service areas, both within research centers and in medical centers and other health care delivery venues.

Kaiser Permanente has extensive experience with issues connected to patient care, research, and health care costs. In particular, and as described more fully below, Kaiser Permanente has firsthand experience with the negative effects that flow from granting patent rights on human genes, including specifically the BRCA1 and BRCA2 genes at issue in this case.

STATEMENT OF THE CASE

As framed in the petition, this case presents the question whether human genes are patentable.

Petitioners brought this case to challenge the validity and constitutionality of seven patents owned by respondents Myriad Genetics, Inc. and the University of Utah Research Foundation (collectively, "Myriad"). Three of those patents are the subject of the petition.[4] The challenged claims of these three

[4] The relevant claims of the three patents still at issue are directed to compositions of matter that petitioners argue are ineligible for patent protection under 35 U.S.C. § 101. The other four patents were directed to processes; the district court and the court of appeals held all but one of the challenged method claims in those patents to be ineligible subject matter

patents are all directed to isolated molecules of deoxyribonucleic acid ("DNA") corresponding to one of two human genes known as BRCA1 and BRCA2. These two genes are among the approximately 25,000 that comprise the human genome found in nearly every cell of the human body. Mutations in the DNA sequences of the BRCA1 and BRCA2 genes are associated with increased risk of breast and ovarian cancer.

Collectively, Myriad's patents claim both the normal (or "wild-type") versions of the BRCA1 and BRCA2 genes and all possible variations and mutations of those genes, known or unknown. *See* Pet. App. 181a, 307a-308a. The claims are limited only by the requirement that these genes be "isolated" — that is, removed from a cell and separated from other genetic material. Isolation of a gene is achieved through the application of standard techniques known in the scientific and medical communities; Myriad claims no intellectual property right in the actual methods of isolation. Instead, Myriad's patents claim the human DNA that has been "isolated" from its cellular environment by application of those methods. Due to the breadth of its patent claims, as noted in the petition, "Myriad claims ownership of the BRCA1 and BRCA2 genes of every American." Pet. 8. The patents have allowed Myriad to establish and enforce a monopoly on clinical testing for BRCA1 and BRCA2 mutations. Moreover, as the exclusive provider of this testing, Myriad has complete control over the resulting data that could otherwise be used by researchers to advance understanding of the

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under § 101. *See* Pet. App. 53a-60a, 224a-236a. The petition does not seek review of the court's holding that one of the method claims is directed to patent-eligible subject matter. *See* Pet. 7 n.2.

precise role these genes play in increasing cancer risk. Myriad's patents entitle it not only to charge a licensing fee for this research but also to control who may conduct it and under what circumstances.

The critical question presented by this case is whether the kind of monopoly enjoyed by Myriad and other gene patent owners is lawful. Under 35 U.S.C. § 101, an inventor may obtain a patent for "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." This Court has long interpreted § 101 to exclude three categories that are outside the otherwise "wide scope" of patent-eligible subject matter: "The laws of nature, physical phenomena, and abstract ideas have been held not patentable." *Diamond v. Chakrabarty*, 447 U.S. 303, 308-09 (1980). Genes as they exist in the human body, for example, are "products of nature" not eligible for patent protection. They are instead "part of the storehouse of knowledge of all men . . . [,] free to all men and reserved exclusively to none." *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948).

The question raised by Myriad's patents is whether these genes may nonetheless be "reserved exclusively" to a single owner if they are isolated from their native cellular environment. Under this Court's precedent, the answer turns on whether the isolated genes have "markedly different characteristics from any found in nature." *Chakrabarty*, 447 U.S. at 310.

The district court applied that test and concluded that isolated DNA is not patentable subject matter under § 101. Granting summary judgment in favor of petitioners, the district court emphasized that simply isolating DNA from its natural state does not change the "fundamental quality of DNA as it exists

in the body" — namely, the critical biological information contained within the DNA. Pet. App. 120a.

Myriad appealed this decision, and a divided panel of the court of appeals reversed. Each member of the panel wrote separately. Judge Lourie, writing for the majority, held that an isolated gene is "markedly different" from a native gene under *Chakrabarty* because the breaking of covalent chemical bonds gives the isolated DNA molecule a "distinctive chemical identity and nature." *Id.* at 45a. Judge Moore, in a separate concurring opinion, agreed that differences in chemical structure are relevant to patentability but found it necessary also to analyze "whether these differences impart a new utility which makes the molecules markedly different from nature." *Id.* at 76a (Moore, J., concurring in part). Judge Moore answered this question in the affirmative, concluding that isolated DNA has practical applications in research and diagnostics for which native DNA is unsuitable. Judge Bryson, dissenting from this part of the majority's ruling, explained of the isolated DNA molecules covered by Myriad's patents that "[t]he only material change made to those genes from their natural state is the change that is necessarily incidental to the extraction of the genes from the environment in which they are found in nature." *Id.* at 98a (Bryson, J., concurring in part and dissenting in part). He opined that the extraction process alone does not render isolated DNA "markedly different" from native DNA and specifically rejected the notion that there is some "magic to a chemical bond that requires us to recognize a new product when a chemical bond is created or broken, but not when other atomic or molecular forces are altered." *Id.* at 99a.

Petitioners seek review of the panel majority's holding with respect to the patent-eligibility of isolated DNA. Although the petition also asks this Court to review other aspects of the appellate court's ruling, including threshold issues related to standing, *amicus* Kaiser Permanente's interest and experience are focused on the substantive question whether Myriad's patent claims and others like them are directed to eligible subject matter under 35 U.S.C. § 101.

REASONS FOR GRANTING THE WRIT

The Court should grant the petition for a writ of certiorari because the Federal Circuit has decided a question of signal importance in patent law that should be reviewed by this Court.[5] More than 30 years have passed since this Court last addressed the patentability of compositions of matter under 35 U.S.C. § 101. The Court has never applied that statute to determine whether human genetic material may be patented.

That question is of paramount importance to the medical and scientific communities. As discussed in more detail below, Kaiser Permanente's experience with the Myriad patents at issue in this case demonstrates the significant negative effects on patient care, diagnostic expertise, genetic research, and medical decisionmaking that flow from granting a patent monopoly on human genes. These negative effects will persist (and likely increase) under the

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[5] As set forth in the petition, this case also merits this Court's review because the court of appeals misapplied this Court's jurisprudence interpreting § 101. *See* Pet. 25-30. In this brief, however, *amicus* Kaiser Permanente will focus on the reasons why gene patentability is an important question of federal law that this Court should decide.

ruling of the court of appeals. The correctness of that ruling is a question that merits consideration by this Court.

I. PATENTS ON ISOLATED DNA DELAY IMPROVEMENTS TO CLINICAL CARE AND IMPEDE CRITICAL GENETIC RESEARCH

Advocates of gene patents — including several *amici* that supported Myriad in the court of appeals — frequently argue that continued innovation in the field of genetics depends on the availability of these patents. They cite the investment required to support cutting-edge genetic research and claim that, but for the prospect of patent exclusivity and the profits it entails, funding would not be forthcoming and research would stall. But Kaiser Permanente's experience with the Myriad patents teaches that the opposite is true: granting patent rights in isolated human genes inhibits both clinical treatment and scientific research and understanding.

Myriad's monopoly on the BRCA1 and BRCA2 genes extends not only to the actual clinical testing for mutations in those genes but also to the use of the data compiled from test results. As the district court found, Myriad is the sole provider of BRCA1 and BRCA2 tests in the United States. *See* Pet. App. 129a. Health care providers such as Kaiser Permanente must rely exclusively on Myriad to test patients' DNA samples for BRCA1 and BRCA2 mutations. Myriad maintains a proprietary database containing the results of all of these tests — a valuable store of information about known malignant variants in the genes as well as variants whose effects are currently unknown. If this information were available to doctors and genetic counselors, it would enhance medical decisionmaking because these pro-

viders could more easily place an individual patient's test results in context and provide more valuable diagnostic information and advice to patients.

But Myriad's patents allow it to deny outside access to this "proprietary" information about the content of individuals' DNA. Kaiser Permanente is barred from obtaining full information about its own members' test results. Instead, Myriad offers summaries of these data upon request and only with a signed release from a clinician. Kaiser Permanente would compile a database of information learned from the test results of its own members — a next-best alternative to accessing the complete Myriad database — but the selective summary data provided by Myriad do not enable it to do so.

Furthermore, if clinicians and researchers outside of Myriad were permitted to access and analyze the full information in Myriad's database, they could use it to develop a more complete understanding of the universe of BRCA1 and BRCA2 mutations and variants and the role these genetic factors play in increasing susceptibility to breast and ovarian cancer. As just one example, researchers outside Myriad could verify whether a particular variant of the BRCA genes is actually linked to cancer risk or is instead benign. The consequence of Myriad's patents and the resulting monopoly on BRCA1 and BRCA2 testing is a broader monopoly on information that patients and their physicians may obtain about the contents of an individual's own DNA, including the patient's own heightened risks of life-threatening disease.

Myriad's patents also have direct negative effects on genetic research and understanding. Myriad claims ownership of the BRCA1 and BRCA2 gene

sequences, but these genes are a small part of the complete human genome. It is well known that most genes do not work alone but rather interact with one or more other genes contained in the genome to produce morphological changes. A researcher studying larger DNA sequences or even the entire genome may discover potential effects that implicate the BRCA1 and BRCA2 genes but also involve other portions of the full genome sequence. The researcher may be compelled to avoid using or disclosing this potentially crucial information for fear of treading upon Myriad's intellectual property rights, even if the new discovery is not limited to the BRCA1 or BRCA2 genes. *See* U.S. Dep't of Health & Human Services, *Report of the Secretary's Advisory Comm. on Genetics, Health, and Society: Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* 49-62 (Apr. 2010) (describing obstacles to whole-genome sequencing presented by gene patents), *available at* http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_patents_report_2010.pdf. This is true not only of the specific genes patented by Myriad, but of *all* patents on isolated human DNA. *See id.* at 50-52. The combined effect of these patents could lead to fragmented ownership of the human genome, with researchers unable to engage in meaningful analysis or scientific dialogue for fear of violating any number of patents.

Judge Bryson recognized this problem in his opinion dissenting from the court of appeals majority. Broadly written patents claiming human genetic material may stall genomic research because, "[i]n order to sequence an entire genome, a firm would have to license thousands of patents from many different licensors. Even if many of those patents

include claims that are invalid for anticipation or obviousness, the costs involved in determining the scope of all of those patents could be prohibitive." Pet. App. 109a (citation omitted).

II. PATENTS ON ISOLATED DNA INCREASE THE COSTS AND REDUCE THE UTILITY OF DIAGNOSTIC GENETIC TESTS

Patents on isolated DNA obstruct the critical research that will lead to advances in clinical understanding and improvements in future diagnostic ability, but more importantly they also prevent patients from receiving the best diagnostic information available now. In several different ways, the patentee's monopoly on testing for the DNA sequence in question reduces both the quantity and quality of information available to patients who need to make well-informed decisions about their health and health care.

The Myriad patents at issue in this case have already produced such negative effects on patient health. As the district court noted, Myriad has asserted its patent rights to prohibit other laboratories from offering diagnostic BRCA1 and BRCA2 testing using isolated DNA. *See* Pet. App. 163a-166a. Health care providers like Kaiser Permanente have no choice but to rely on Myriad to test patients' DNA samples for mutations to the BRCA1 and BRCA2 genes. Since 1997, when the patents-in-suit took effect, Kaiser Permanente has ordered BRCA1 and BRCA2 testing for its members exclusively through Myriad.

Kaiser Permanente is committed to offering its members and patients the best possible medical care; when a genetic specialist determines that a test should be ordered for a Kaiser Permanente member,

it will pay the high rates that Myriad is able to charge for its exclusive diagnostic services. But even this is no guarantee that patients will receive the full benefit of genetic testing. A clinician counseling a patient at risk for hereditary cancer will want to test the family member most likely to have a genetic mutation first, in order to identify the specific mutation carried in the family and then use a more targeted test to analyze the DNA samples of other family members (often at one-tenth the cost of the comprehensive test). Thus, the clinician may identify the patient's parent, sibling, or other relative as the primary candidate for genetic testing. If the patient's relative is not also a covered Kaiser Permanente member, however, there is no guarantee that testing will be feasible. The cost of each test can exceed $3,000. The relative may have no medical insurance, or may have insurance that does not cover Myriad's tests, and the high price tag is often prohibitive.

In this scenario, Kaiser Permanente still offers testing to its member patient, but the test is of limited value without a clear, complete picture of the familial cancer risk. For example, consider a Kaiser Permanente patient who has no personal history of breast cancer and whose individual risk for a BRCA1 or BRCA2 mutation is comparatively low, but whose family history strongly suggests hereditary cancer susceptibility. While testing only the patient herself will assist with that patient's care, the patient is likely to produce a negative result because of her low individual risk. This negative result is of limited use in isolation. By contrast, if the family member most at risk for a mutation is tested and the mutation is found in that family member, other relatives have an

incentive to get tested — and those who test negative for the same mutation can be certain that they are free of the familial risk.

Kaiser Permanente's genetics counselors and clinicians need access to this kind of complete familial information to provide the best advice to patients concerning their overall cancer risk, need for surveillance, and candidacy for elective prophylactic surgeries, including mastectomies. The Myriad patents and the diagnostic monopoly often make it practically impossible for Kaiser Permanente to do so.

If Myriad (or any other entity) did not have patent rights to the isolated BRCA1 and BRCA2 genes, other facilities would be able to test for mutations in those genes. Having multiple providers may lead to competitive pricing; lower costs would mean more widespread availability and the ability to obtain a "second opinion" by having another facility perform a confirmatory test. Having multiple providers may also mean that a wider range of testing options is available, rather than the particular tests a monopoly provider chooses to offer. These benefits are possible with other diagnostic tests that are not restricted by gene patents. For example, while Myriad offers tests screening for colo-rectal cancer, it does not have a patent on the affected gene sequences. Other laboratories can therefore offer screening tests, and many do so at a lower price than Myriad, to the ultimate benefit of patients and consumers as well as public and private healthcare payers.

In fact, but for the Myriad patents, Kaiser Permanente would work to obtain the facilities necessary to conduct BRCA1 and BRCA2 screening internally, which would dramatically reduce the costs of testing and would therefore make it easier to offer screen-

ing to the most appropriate candidates, including relatives of Kaiser Permanente members who are identified as being most at-risk for an inherited gene mutation. In addition, Kaiser Permanente would have more control over the testing process and would be able to select the most appropriate test for any given individual, rather than relying on the set menu of choices that Myriad has elected to offer.

III. PATENTS ON ISOLATED DNA CONFLICT WITH PHYSICIANS' ETHICAL OBLIGATIONS TO PATIENTS

Finally, the patentability of isolated human genes can create serious ethical conflicts for physicians. Advances in technology are making it possible to sequence a patient's entire genome or exome (the active portions of the genome), rather than just testing for variations in the sequence of a particular gene. *See* Pet. App. 109a. As discussed above in Part I, the issuance of patents on numerous individual genes presents serious obstacles to researchers seeking to study the full genome sequence. These challenges are even more problematic for laboratories and clinicians looking at a patient's genome or exome for diagnostic purposes. Even if not testing specifically for variations in a patented gene sequence, such as BRCA1 or BRCA2, the clinician may see such a variation when analyzing the genome or exome in full. The clinician is then presented with a dilemma: whether to disclose the variation to the patient and risk violating the patent owner's intellectual property rights, or not disclose that the patient has a genetic risk of developing cancer (or any other disease that may be implicated by gene patents).

CONCLUSION

Because the judgment below raises an important issue of patent law with wide-ranging consequences to health care providers, certiorari is warranted. The petition for a writ of certiorari should be granted.

Respectfully submitted,

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